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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,130	02/05/2002	Olga Bandman	PF-0319-2 DIV	2603
27904	7590	02/24/2004	EXAMINER	
INCYTE CORPORATION 3160 PORTER DRIVE PALO ALTO, CA 94304			STEADMAN, DAVID J	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/072,130

Applicant(s)

BANDMAN ET AL.

Examiner

David J Steadman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,11,12 and 29-45 is/are pending in the application.
- 4a) Of the above claim(s) 1,12,29,30,33,35,44 and 45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11,31,32,34 and 36-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

[1] Due to an editing error in the Advisory action mailed December 10, 2003, the examiner inadvertently withdrew the written description and scope of enablement rejections of claim 11 part b) (see items [8] and [9]). As the rejections were inadvertently withdrawn, the rejections are being re-instated herein and the finality of the Office action mailed August 26, 2003 is withdrawn.

[2] Applicants' amendment to the claims, filed February 02, 2004, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Claims 1, 11-12, and 29-45 are pending in the application.

[4] Claims 1, 12, 29-30, 33, 35, and 44-45 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

[5] Claims 11, 31-32, 34, and 36-43 are being examined on the merits.

[6] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, First Paragraph

[7] Claims 11, 31-32, 34, 36-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. It is noted that, upon further consideration, claims 34 and 36-41 are being included in the instant rejection for the reasons stated below. It should also be noted that the instant rejection applies to all

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parts of claim 11, *i.e.*, parts a) to d). The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention.

The claims are drawn to a genus of isolated antibodies. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses a single representative species of the claimed genus of antibodies, *i.e.*, an antibody the binds the polypeptide of SEQ ID NO:1. Other than this SINGLE disclosed species of the claimed genus, the specification fails to describe any additional species, which in this case encompasses species that are WIDELY variant, including (but not limited to) any antibody that binds an epitope that is present at the N- or C- terminus of a polypeptide *with* or *comprising* SEQ ID NO:1 or variants thereof, *i.e.*,

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an antibody that binds any amino acid sequence that is outside of the sequence of SEQ ID NO:1 that is present in a polypeptide *with* or *comprising* SEQ ID NO:1. As such, the disclosure of the single representative species as stated above is insufficient to be representative of the attributes and features of *all* species encompassed by the claimed genus of chimeric nucleic acids. Given the lack of description of a representative number of chimeric nucleic acids, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

Applicants argue the term "comprising" has been replaced by the term "with" to address the instant rejection. However, it is noted that the term "with" has been interpreted as "inclusive or open-ended" and as not excluding additional unrecited elements (see MPEP 2111.03), particularly as there is no evidence of record that would suggest that the term "with" should be interpreted as closed claim language, and therefore, the term does not limit the sequence of the recited polypeptide to SEQ ID NO:1. As such, the polypeptide to which the genus of claimed antibodies can bind is unlimited with respect to additional amino acids that are present at the N- and/or C-terminus in a polypeptide *with* or *comprising* SEQ ID NO:1.

[8] Claim(s) 11, 31-32, 34, 36-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody that binds to SEQ ID NO:1, does not reasonably provide enablement for all antibodies that bind to a polypeptide *with* or *comprising* SEQ ID NO:1 or variants or fragments thereof as encompassed by the claims. The specification does not enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. It is noted that, upon further consideration, claims 34 and 36-41 are being included in the instant rejection for the reasons stated below. It should also be noted that the instant rejection applies to all parts of claim 11, *i.e.*, parts a) to d).

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

- The claims are overly broad in scope: The claims are so broad as to encompass all antibodies that bind to a polypeptide *with or comprising* SEQ ID NO:1 or variants or fragments thereof as broadly encompassed by the claims. The broad scope of claimed antibodies is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of antibodies broadly encompassed by the claims. The claims are not limited to an antibody that binds SEQ ID NO:1 and instead

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encompass antibodies that bind polypeptides with or comprising the amino acid sequence of SEQ ID NO:1, including antibodies that bind amino acids at the N- or C-terminus of SEQ ID NO:1. In this case the enablement provided by the disclosure is limited to an antibody that binds to SEQ ID NO:1.

- The lack of guidance and working examples: The specification provides only a single working example of the claimed antibody, *i.e.*, an antibody that binds SEQ ID NO:1. This single working example fails to provide the necessary guidance for making and/or using the broad scope of claimed antibodies. The specification provides no guidance for altering the amino acid sequence of SEQ ID NO:1, *e.g.*, by altering SEQ ID NO:1 itself and/or addition of amino acids at the N- and/or C-terminus with an expectation that the antibody will maintain the ability to bind SEQ ID NO:1.
- The high degree of unpredictability in the art: The ability of an antibody to bind a particular epitope within a polypeptide is dependent upon the amino acid sequence of the polypeptide and, if the polypeptide is in its native state, *i.e.*, non-denatured, the resulting conformation acquired by the amino acid sequence (see Abaza et al. *J Protein Chem* 11:433-444 who teach that "the reaction of a protein antigen with its antibodies is influenced by conformational changes" (page 436, left column, bottom to right column, top)). It is highly unpredictable as to which alterations in a protein's amino acid sequence can be made with an expectation of maintaining the ability of an antibody to bind the altered polypeptide sequence.

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- The state of the prior art supports the high degree of unpredictability: The state of the art provides evidence for the high degree of unpredictability that an antibody, e.g., an antibody that binds SEQ ID NO:1, will bind to an altered polypeptide sequence, e.g., variants of SEQ ID NO:1 or SEQ ID NO:1 with additional amino acids at the N- and/or C-terminus. For example, Colman et al. (*Res Immun* 145:33-36) teach that “[s]ingle amino acid changes within the interface of an antibody-antigen complex... ..can effectively abolish the interaction entirely” (page 33, right column). Furthermore, Abaza et al. (*J Protein Chem* 11:433-444) teach that alterations outside of the boundaries of an antigenic site can significantly affect antibody binding (page 443, right column to page 444, left column).
- The amount of experimentation required is undue: While methods of generating antibodies against a known antigen are known, it is not routine in the art to generate antibodies that bind amino acid sequences having a substantial number of modifications, as encompassed by the instant claims. Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)).

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Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants argue the term "comprising" has been replaced by the term "with" to address the instant rejection. However, it is noted that the term "with" has been interpreted as "inclusive or open-ended" and as not excluding additional unrecited elements (see MPEP 2111.03), particularly as there is no evidence of record that would suggest that the term "with" should be interpreted as closed claim language, and therefore, the term does not limit the sequence of the recited polypeptide to SEQ ID NO:1. As such, the polypeptide to which the genus of claimed antibodies can bind is unlimited with respect to additional amino acids that are present at the N- and/or C-terminus in a polypeptide *with* or *comprising* SEQ ID NO:1.

Conclusion

[9] Status of the claims:

- Claims 1, 11-12, and 29-45 are pending.
- Claims 1, 12, 29-30, 33, 35, and 44-45 are withdrawn from consideration.
- Claims 11, 31-32, 34, and 36-43 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's

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supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

Patent Examiner

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AS 02-20-04